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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/758,017	01/10/2001	Olav Lanes	U 013209-3	8104

7590

06/02/2003

Ladas & Parry
26 West 61st Street
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EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
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1652

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DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n N .

09/758,017

Applicant(s)

LANES ET AL.

Examiner

Elizabeth Slobodyansky

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 March 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 19.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

The amendment filed March 10, 2003 amending the specification to correct references to the sequence identifiers, canceling claims 1-16 and adding claims 17-29 has been entered.

The substitute Sequence Listing has been filed March 10, 2003. Upon examiner's request Applicants provided on May 30, 2003 an additional copy of the computer readable form (CRF) thereof. Both, the paper copy and CRF, have been entered.

Claims 17-29 are pending.

Election/Restriction

Newly submitted claims 17-29 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claims encompass an additional enzyme with the amino acid sequence of SEQ ID NO:4. Inventions drawn to SEQ ID NO:2 and SEQ ID NO:4 are independent and patentably distinct. The polypeptides of SEQ ID NO:2 and SEQ ID NO:4 represent structurally different enzymes. Therefore, where structural identity is required, such as for production of antibodies or pharmacological action, the different sequences have different effects.

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Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 17-29 in part drawn to SEQ ID NO:4 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Drawings

The drawings filed on March 10, 2003 have been approved by Draftsman.

Specification

The disclosure is objected to because of the following: It refers to the amino acid sequences as SEQ ID NOs: 1 and 2 where it appears SEQ ID NOs:2 and 4 are intended (page 27, line 13, for example). It refers to "a nucleotide sequence as given in SEQ ID NOs: 2 or 4" where it appears SEQ ID NOs:1 and 3 are intended (page 8, paragraph 2).

The amendment filed March 10, 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The Sequence Listing filed March 10, 2003 contains changes as compared to the Sequence Listing

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filed January 29, 2002 that is currently present in the application. The changes are at least as follows: Serine at position 125 in SEQ ID NO:2 has been changed to Tryptophane; the total number of sequences has been changed from 19 to 22. No explanation for the changes is given.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

Claim 18, with dependent claims 20, 22, 24, 26, 28, is objected to under 37 CFR 1.75(d)(1) as being in improper form because the claim states an improper Markush group. Compounds included within a Markush group must (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility (See MPEP 803.02.) While the structures recited in claim 18 may share the common utility of a thermolabile uracyl-DNA glycosylase, the specification does NOT disclose that SEQ ID NO:2 and SEQ ID NO:4 share a substantial structural feature disclosed as being essential to that utility. Because a substantial structural feature is not disclosed as being essential to the utility that is common to the claimed species, the claim states an improper Markush group.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-20, 22-24 and 26-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 18 recites SEQ ID NO:2 that was amended to replace Serine at position 125 with Tryptophane.

Claims 18 and 19 recite "ectothermal organism" and "temperatures below 10° C". The Examiner is unable to locate adequate support in the specification for such limitations. Thus, there is no indication that S125W replacement in SEQ ID NO:2 and limitations "ectothermal organism" and "temperatures below 10° C" were within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

Claims not specifically rejected herein are rejected as dependent from the rejected claim.

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Claims 17, with dependent claims 19, 21, 23, 25, 27 and 29, is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 17, with dependent claim 29, is directed to an uracil-DNA glycosylase (UNG) that is completely inactivated above 60° C from any source, both naturally-occurring and man made. Claim 19 limits the source of an uracil-DNA glycosylase to "ectothermal organism adapted to environmental temperatures below 10° C". Claims 21 and 23 limit the source of an uracil-DNA glycosylase to "eukaryotic organism". Claims 25 and 27 limit the source of an uracil-DNA glycosylase to "Atlantic cod (*Gadus morhua*)".

The claimed genus of uracil-DNA glycosylases encompasses not only the disclosed species but many other proteins as well since some, for example mammalian proteins, commonly have allelic and splicing variants which are encoded by the same gene and different genes can encode proteins with the same function (e.g., specification, page 2, lines 18-23). All such allelic and splicing variants are encompassed by the claims. While claims 25 and 27 limit the enzymes to UNGs naturally-occurring in Atlantic cod, SEQ ID NO:2 and SEQ ID NO:4 are insufficient to describe and/or predict the structure of other naturally-occurring allelic and splicing

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variants even if they are encoded by the same gene. Applicants disclose two representative species of the claimed genus, an uracil-DNA glycosylase from Atlantic cod having the amino acid sequences of UNG1 and UNG2, SEQ ID NOs: 2 and 4, respectively. However, absent a disclosure of the structural features common to the species within the genus, the description of two species is not sufficient as the description of the entire genus. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being an uracil-DNA glycosylase that is completely inactivated above 60° C. The functional definition of the genus does not provide any structural information or other identifying characteristics commonly possessed by members of the genus that would allow one to recognize and/or predict a structure of other members of the genus. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Response to Arguments

Applicant's arguments filed March 10, 2003 have been fully considered but they are not persuasive.

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Applicants argue that "SEQ ID NO:2 and SEQ ID NO:4 are the amino acid sequences that correspond to SEQ ID Nos: 1 and 2 of the original sequence listing. The PatentIn software automatically generates a separate sequences for the amino acid when the preceding sequence is for the DNA and the amino acid coded for by the DNA" (Remarks, page 4). This is not persuasive because while it is unclear which Sequence Listing Applicants consider as the original, the point of the objection is that the sequence search performed at the USPTO shows the discrepancy between SEQ ID NOs: 2 (UNG1) and 4 (UNG2) of the instant application (Sequence Listing filed January 29, 2002) and the sequences of UNG1 and UNG2 in WO 200151623. For example, SEQ ID NO:2 has Serine at position 125 while UNG1 in WO 200151623 has Tryptophane at the same position. WO 200151623 is based on the same the priority applications NO 2000 0163 and NO 2000 5428 as the instant application.

Applicants assert with regard to UNG1 and UNG 2 that absent N-terminal sequences "The resulting proteins are identical, and encompass the catalytic domain" (page 4, emphasis added). The examiner notes that said sequences as filed on January 29, 2002 are not identical and contain 14 mismatches within amino acid residues 33-301.

If Applicants seek to amend the Sequence Listing based on the foreign priority documents, they should provide a detailed explanation and the alignment of the relevant sequences.

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With regard to the written description, Applicants argue that they describe “the first eukaryote UNG that also is thermolabile and not able to reactivate” (page 5, 1st sentence). They further assert that “The primary sequence for UNG enzymes are particularly well conserved among vertebrates with 80-90% sequence identity in the catalytic domain between fish and mammals. ... Considering the high sequence identity within the vertebrates, it must therefore be considered very likely that the primary structure (amino acid sequence) that is common to this group also determines the inability of enzymes from this group to refold” (page 5). This is not persuasive because other eukaryotic UNGs are not thermolabile in spite of the sequence homology between the species. It is the point of the rejection that the structure imparting the thermolability that is common to all members of the genus is not disclosed. Applicants do not teach which residues in the sequence are responsible for thermolability while conceding that “The heat lability of the Cod enzyme is determined by a limited number of amino acid substitutions in the Cod enzyme compared to other vertebrate UNGs” (page 5). However, this “limited number of amino acid substitutions in the Cod enzyme” is not taught by the specification.

The 112, 2nd paragraph, and 101 rejections are withdrawn in view of the amendment.

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Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

Elizabeth Slobodyansky, PhD
Primary Examiner

May 30, 2003